L Number	Hits	Search Text	DB	Time stamp
1	2	6160088.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/04 15:33
7	2	KDEL adj receptor adj inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/04 15:38
13	13	KDEL adj receptor and inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/04 16:31
19	156	(endoplasmic adj reticulum) near4 (retention) near4 (signal or receptor)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/04 16:35
25	0	((endoplasmic adj reticulum) near4 (retention) near4 (signal or receptor)) near4 (inhibitor or antagonist)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/04 16:36

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AN 2001:269558 BIOSIS
DN PREV200100269558
TI **KDEL receptor inhibitors**.
AU Rothman, James E. (1); Mayhew, Mark; Hoe, Mee H.
CS (1) New York, NY USA
    ASSIGNEE: Sloan-Kettering Institute For Cancer, New York, NY, USA
PI US 6160088 December 12, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 12, 2000) Vol. 1241, No. 2, pp. No Pagination. e-file.
    ISSN: 0098-1133.
DT Patent
LA English
AB The present invention relates to **inhibitors** of the **KDEL receptor** and therapeutic uses therefor. Certain proteins are functionally retained in the cellular endoplasmic reticulum via an interaction between a KDEL sequence and its receptor. According to the invention, blocking this interaction with a **KDEL receptor inhibitor** promotes the secretion of such proteins. In specific embodiments of the invention, **KDEL receptor inhibitors** may be used to promote the secretion of heat shock proteins, thereby rendering the secreted heat shock proteins more accessible to the immune system and improving the immune response to heat shock protein-associated antigens.

L2 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

AN 2000:98760 CAPLUS
DN 132:133894
TI Inhibition of KDEL receptor-mediated return of heat shock protein complexes to the endoplasmic reticulum and their adjuvant use
IN Rothman, James E.; Mayhew, Mark; Hoe, Mee H.
PA Sloan-Kettering Institute for Cancer Research, USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	US 6160088	A	20001212	US 1998-124671	19980729
	AU 9953245	A1	20000221	AU 1999-53245	19990728
	EP 1100906	A1	20010523	EP 1999-938851	19990728
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1998-124671	A	19980729		
	WO 1999-US17147	W	19990728		

AB **Inhibitors** of the **KDEL receptor** that can be used to block the transfer of heat shock proteins to the endoplasmic reticulum and allow them to act as adjuvants are described. Certain proteins are functionally retained in the cellular endoplasmic reticulum via an interaction between a KDEL sequence and its receptor. According to the invention, blocking this interaction with a **KDEL receptor inhibitor** promotes the secretion of such proteins. In specific embodiments of the invention, **KDEL receptor inhibitors** may be used to promote the secretion of heat shock proteins, thereby rendering the secreted heat shock proteins more accessible to the immune system and improving the immune response to heat shock protein-assocd. antigens. The inhibitors are artificial peptides that oligomerize and present large no. of KDEL peptides to the receptors and sat. them. An example of one of these peptides uses the signal peptide of the BiP protein, an oligomerization domain of a cartilage oligomeric matrix protein, a linker peptide from a camel Ig and a KDEL peptide is described.

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TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion or proteins which are normally retained within the cell;
herpes simplex virus-based vector e.g. plasmid pHSV1, retro virus vector and Moloney retro virus vector-mediated expression in transgenic animal for infectious disease and cancer therapy
AU Rothman J E; Mayhew M; Hoe M H
PA Sloan-Kettering-Inst.Cancer-Res.
LO New York, NY, USA.
PI WO 2000006729 10 Feb 2000

AI WO 1999-US17147 28 Jul 1999
PRAI US 1998-124671 29 Jul 1998
DT Patent
LA English
OS WPI: 2000-195296 [17]
AB An oligomeric **KDEL receptor inhibitor** protein which promotes secretion of proteins normally retained within the cell is new. The inhibitor protein contains several subunits where each subunit contains an oligomerization domain and has at its carboxy terminus a region which binds to a KDEL receptor. Also claimed are: a nucleic acid encoding the **KDEL receptor-inhibitor**; a non-human transgenic animal carrying a transgenic **KDEL receptor inhibitor** protein linked to a promoter sequence; increasing the secretion of a protein by a cell; promoting the release of heat shock protein/antigenic peptide complex from a cell; and inducing or increasing an immune response to a target antigen. Vectors include herpes simplex virus based vectors e.g. plasmid pHSV1, retro virus vectors e.g. MFG and in particular Moloney retro virus vectors such as LN, LNSX, LNCX and LXSN. The KDEL receptors can be used to promote secretion of proteins such as heat shock proteins thereby making them more accessible to the immune system and improving the immune response. The methods may be used for treating infectious disease or cancer. Secretion of genetically engineered proteins may also be achieved. (87pp)

L2 ANSWER 4 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44970 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is a targeting peptide termed RGD-4C. This may be incorporated into the amino terminal region of a **KDEL receptor inhibitor** protein downstream from a cleavably removed sequence to improve its activity or alter its immunogenicity.

L2 ANSWER 5 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44969 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.

PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is a detectably labeled peptide which binds the erd 2 receptor. The ability of a putative **KDEL receptor inhibitor** to bind to the erd 2 receptor may be determined by measuring the ability of the inhibitor to compete with this labeled peptide.

L2 ANSWER 6 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44968 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is a detectably labeled peptide which binds the erd 2 receptor. The ability of a putative **KDEL receptor inhibitor** to bind to the erd 2 receptor may be determined by measuring the ability of the inhibitor to compete with this labeled peptide.

L2 ANSWER 7 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44967 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.

PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; a myc-tag; an N-glycosylation sequence; the oligomerisation domain of rat cartilage oligomeric matrix protein (COMP); a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat COMP which provides increased stability via disulphide bonds.

L2 ANSWER 8 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44966 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human thrombospondin 4 (TSP4) trimerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 9 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44965 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -

IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human thrombospondin 3 (TSP3) trimerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 10 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44964 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human phospholamban (PLB) pentamerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 11 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44963 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which

comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human cartilage oligomeric matrix protein (COMP) pentamerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat COMP which provides increased stability via disulphide bonds.

L2 ANSWER 12 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44962 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of Xenopus thrombospondin 4 (TSP4) trimerisation domain including an additional subsequence; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 13 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44961 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of mouse thrombospondin 3 (TSP3) trimerisation domain including an additional subsequence; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 14 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44960 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of mouse thrombospondin 3 (TSP3) trimerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL.

The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 15 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44959 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** protein comprising regions including a cleavable signal peptide; the oligomerisation domain from rat cartilage oligomeric matrix protein (COMP); a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat COMP which provides increased stability via disulphide bonds.

L2 ANSWER 16 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44958 Protein DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is **KDEL receptor inhibitor** protein comprising regions including a cleavable signal

peptide; the oligomerisation domain from rat cartilage oligomeric matrix protein; a camel IgG linker domain and the carboxy-terminal sequence KDEL.

L2 ANSWER 17 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44957 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human papillomavirus antigenic peptide. This serves as the target antigen for compositions comprising a **KDEL receptor inhibitor**. The target antigen forms a complex with a heat shock protein and the heat shock protein contains a ligand sequence which binds to a KDEL receptor.

L2 ANSWER 18 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44956 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human papillomavirus antigenic peptide. This serves as the target antigen for compositions comprising a

KDEL receptor inhibitor. The target antigen forms a complex with a heat shock protein and the heat shock protein contains a ligand sequence which binds to a KDEL receptor.

L2 ANSWER 19 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44955 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human papillomavirus antigenic peptide. This serves as the target antigen for compositions comprising a **KDEL receptor inhibitor**. The target antigen forms a complex with a heat shock protein and the heat shock protein contains a ligand sequence which binds to a KDEL receptor.

L2 ANSWER 20 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44954 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human papillomavirus antigenic peptide. This serves as the target antigen for compositions comprising a

KDEL receptor inhibitor. The target antigen forms a complex with a heat shock protein and the heat shock protein contains a ligand sequence which binds to a KDEL receptor.

L2 ANSWER 21 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44953 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human papillomavirus antigenic peptide. This serves as the target antigen for compositions comprising a **KDEL receptor inhibitor**. The target antigen forms a complex with a heat shock protein and the heat shock protein contains a ligand sequence which binds to a KDEL receptor.

L2 ANSWER 22 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44952 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human phospholamban (PLB), a pentameric domain. Oligomers formed via oligomerisation domain of PLB are used to

produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 23 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44951 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is Xenopus thrombospondin 4 (TSP4) trimerisation domain. Oligomers formed via oligomerisation domain of TSP4 are used to produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 24 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44950 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human thrombospondin 4 (TSP4) trimerisation domain. Oligomers formed via oligomerisation domain of TSP4 are used to produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 25 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44949 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human thrombospondin 3 trimerisation (TSP3) domain. Oligomers formed via oligomerisation domain of TSP3 are used to produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 26 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44948 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is mouse thrombospondin 3 (TSP3) trimerisation domain. Oligomers formed via oligomerisation domain of TSP3 are used to produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 27 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44947 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which

comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is human cartilage oligomatrix protein (COMP) pentamerisation domain. Pentamers formed via oligomerisation domain of COMP are used to produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 28 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAY44946 peptide DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence is rat cartilage oligomatrix protein (COMP) pentamerisation domain. Pentamers formed via oligomerisation domain of COMP are used to produce high avidity binding protein which bind to KDEL receptor.

L2 ANSWER 29 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50501 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -

IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; a myc-tag; an N-glycosylation sequence; the oligomerisation domain of rat cartilage oligomeric matrix protein (COMP); a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat COMP which provides increased stability via disulphide bonds.

L2 ANSWER 30 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50500 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human thrombospondin 4 (TSP4) trimerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 31 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50499 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which

comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human thrombospondin 3 (TSP3) trimerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 32 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50498 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human phospholamban (PLB) pentamerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 33 OF 38 DGENE (C) 2002 THOMSON DERWENT

AN AAZ50497 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of human cartilage oligomeric matrix protein (COMP) pentamerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat COMP which provides increased stability via disulphide bonds.

L2 ANSWER 34 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50496 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of Xenopus thrombospondin 4 (TSP4) trimerisation domain including an additional sub-sequence; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which

provides increased stability via disulphide bonds.

L2 ANSWER 35 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50495 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain of mouse thrombospondin 3 (TSP3) trimerisation domain including an additional sub-sequence; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 36 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50494 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide;

the oligomerisation domain of mouse thrombospondin 3 (TSP3) trimerisation domain; a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat cartilage oligomeric matrix protein which provides increased stability via disulphide bonds.

L2 ANSWER 37 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50493 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain from rat cartilage oligomeric matrix protein (COMP); a camel IgG linker domain and the carboxy-terminal sequence KDEL. The subsequence GDCC is an alteration of rat COMP which provides increased stability via disulphide bonds. This is introduced into host cells by suitable vectors.

L2 ANSWER 38 OF 38 DGENE (C) 2002 THOMSON DERWENT
AN AAZ50492 DNA DGENE
TI **Inhibitors** of the **KDEL receptor** which comprises an oligomerization domain useful for promoting secretion of proteins which are normally retained within the cell -
IN Rothman J E; Mayhew M; Hoe M H
PA (SLOK) SLOAN KETTERING INST CANCER RES.
PI WO 2000006729 A1 20000210 87p
AI WO 1999-US17147 19990728
PRAI US 1998-124671 19980729
DT Patent
LA English
OS 2000-195296 [17]
AB The patent discloses the use of **KDEL receptor inhibitor** to promote secretion of proteins that are normally retained within the cell such as heat shock proteins by inhibiting KDEL receptor-mediated return of protein complexes to endoplasmic reticulum. This makes the secreted heat shock proteins more accessible to the immune system and improves immune response to a target antigen. The inhibitor protein comprises several subunits where each subunit comprises an oligomerisation domain and has at its carboxy terminus a region which binds to a KDEL receptor. The target antigen may be associated with diseases including neoplasia such as sarcoma, lymphoma, leukemia, melanoma, carcinoma, glioblastoma and astromytoma, with defective tumour

suppressor genes, oncogenes, infectious diseases, allergy or autoimmune diseases. The present sequence encodes **KDEL receptor inhibitor** comprising regions encoding a cleavable signal peptide; the oligomerisation domain from rat cartilage oligomeric matrix protein; a camel IgG linker domain and the carboxy -terminal sequence KDEL. This is introduced into host cells by suitable vectors.

```
=> s (endoplasmic reticulum) (4A) retention (4a) (signal or receptor)
  13 FILES SEARCHED...
  29 FILES SEARCHED...
  40 FILES SEARCHED...
  47 FILES SEARCHED...
  55 FILES SEARCHED...
  59 FILES SEARCHED...
  85 FILES SEARCHED...
 101 FILES SEARCHED...
L3        1753 (ENDOPLASMIC RETICULUM) (4A) RETENTION (4A) (SIGNAL OR RECEPTOR)


=> s l3 (4A) inhibitor
  32 FILES SEARCHED...
  62 FILES SEARCHED...
 102 FILES SEARCHED...
L4           9 L3 (4A) INHIBITOR

=> s l3 (2S) (inhibitor or antagonist)
  27 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L145 (2S) '
  54 FILES SEARCHED...
  92 FILES SEARCHED...
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L207 (2S) '
L5         114 L3 (2S) (INHIBITOR OR ANTAGONIST)

=> duplicate l5
ENTER REMOVE, IDENTIFY, ONLY, OR (?):remove
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, BIOCOMMERCE, DGENE,
DRUGLAUNCH, DRUGMONOG2, DRUGUPDATES, FEDRIP, FOREGE, GENBANK, KOSMET,
MEDICONF, PHAR, SYNTHLINE, CHEMLIST, HSDB, MSDS-CCOHS, MSDS-OHS, RTECS, CONF,
EVENTLINE, IMSDRUGCONF, DIOGENES, INVESTEXT, USAN, FORIS, FORKAT, UFORDAT,
CHEMINFORMRX, CHEMREACT, DJSMONLINE, CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
DUPLICATE PREFERENCE IS 'AGRICOLA, AQUASCI, BIOSIS, BIOTECHABS, BIOTECHNO, CABA,
CANCERLIT, CAPLUS, DGENE, EMBASE, ESBIOBASE, LIFESCI, MEDLINE, PASCAL, PROMT,
SCISEARCH, TOXCENTER, WPINDEX, NLDB'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L5
L6           57 DUPLICATE REMOVE L5 (57 DUPLICATES REMOVED)

=> d l6 1-57 bib ab

L6   ANSWER 1 OF 57  WPINDEX  (C) 2002 THOMSON DERWENT
AN   2002-331984 [37]   WPINDEX
DNC  C2002-095895
TI   Identifying inhibitor of ubiquitin mediated proteolysis of phosphorylated
     IkappaB, useful for inhibiting NFkappaB activation involves testing
     ability of compound to interfere with beta TrCP/E3RS-hnRNP U interaction.
DC   B04 D16
IN   ALKALAY, I; BEN-NERIAH, Y; BEN-SHUSHAN, E; DAVIS, M; HTZUBAI, A; YARON, A;
     HATZUBAI, A
PA   (YISS) YISSUM RES DEV CO HEBREW UNIV JERUSALEM
CYC  97
PI   EP 1182251    A1 20020227 (200237)* EN   37p
        R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
           RO SE SI
     WO 2002016633 A2 20020228 (200237)  EN
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
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NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002022343 A 20020304 (200247)

ADT EP 1182251 A1 EP 2000-117429 20000811; WO 2002016633 A2 WO 2001-IB2428 20010810; AU 2002022343 A AU 2002-22343 20010810

FDT AU 2002022343 A Based on WO 200216633

PRAI EP 2000-117429 20000811

AB EP 1182251 A UPAB: 20020613

NOVELTY - Identifying (M1) compound that modulates, in particular inhibits, ubiquitin-mediated proteolysis of phosphorylated IkappaB (inhibitor protein of NFkappaB activation), where the compound is tested for its capacity to directly or indirectly modulate, in particular interfere with, ability of beta -TrCP/E3RS (ubiquitin-protein ligase (E3) receptor subunit) to engage in protein-protein association involving hnRNP-U.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) use of a compound that has the capacity to interfere, directly or indirectly, with the ability of beta -TrCP/E3RS to engage in protein-protein association involving hnRNP-U for the preparation of a medicament for the treatment of disorders associated with NF-kappaB activation;

(2) use of a compound that inactivates the hnRNP-U protein per se, for the preparation of a medicament for the treatment of disorders associated with NF-kappaB activation;

(3) anti hnRNP-U antibodies for the diagnosis of condition in which the beta -TrCP/E3RS is compromised, and for monitoring the therapeutic efficacy of an inhibitor of ubiquitin-mediated proteolysis of phosphorylated IkappaB; and

(4) producing a functional beta -TrCP/E3RS, where beta -TrCP/E3RS and hnRNP-U are co-expressed, optionally together with Skp1, in a bacterial, yeast or insect cell.

ACTIVITY - Anti-HIV; immunosuppressive; antibacterial; antirheumatic; antiarthritic; antiasthmatic; cytostatic; nootropic; neuroprotective; cerebroprotective. No biodata is given in the source material.

MECHANISM OF ACTION - Modulator of NFkappaB activation; modulator of ubiquitin-mediated proteolysis of phosphorylated IkappaB; inhibits beta -TrCP/E3RS by inhibiting association of hnRNP-U with E3RS or by inactivating hnRNP-U.

USE - (M1) is useful for identifying a compound that modulates, in particular inhibits ubiquitin-mediated proteolysis of phosphorylated IkappaB (claimed). The beta -TrCP/E3RS inhibitors identified by the above method are useful for preparing medicaments for treating disorders associated with NFkapaB activation such as progression of acquired immunodeficiency syndrome (AIDS); activation of T-cells, B-cells and macrophages during the immune response such as acute phase response; toxic shock, transplant rejection and the response to the cell to gamma radiation and UV light. The E3RS inhibitors are useful as antiinflammatory drugs, and thus useful in the treatment of asthma or rheumatoid arthritis, in cancer therapy in order to increase the sensitivity of the patient to chemotherapeutic agents, in the therapy of central nervous system disorders e.g., neurodegenerative diseases such as Alzheimer's disease, stroke due to atherosclerosis; and as immunosuppressive drugs.

ADVANTAGE - The method requires fewer components than the described E3-substrate interruption assay (i.e., there is no need for any substrate, ubiquitination enzymes,) and therefore the method is simpler and accurate, obviates the need to prepare an IKK-phosphorylated substrate, assay a low affinity complex which is more amenable for interruption, thus allowing the identification of a broader range of inhibitors. The method can also

be applied for identifying inhibitors of cellular targets of human immunodeficiency virus (HIV), and these inhibitors are expected to be superior over the other NFkappaB inhibitors by inhibiting the function of both NFkappaB and Vpu, which are necessary for HIV replication.

DESCRIPTION OF DRAWING(S) - The figure shows Vpu-mediated CD4 degradation assay.

Dwg.7A/7

L6 ANSWER 2 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AN 2002:346537 BIOSIS

DN PREV200200346537

TI Identification of a familial hyperinsulinism-causing mutation in the sulfonylurea receptor 1 that prevents normal trafficking and function of KATP channels.

AU Taschenberger, Grit; Mougey, Adam; Shen, Shu; Lester, Linda B.; LaFranchi, Stephen; Shyng, Show-Ling (1)

CS (1) Center for Research on Occupational and Environmental Toxicology, Oregon Health and Science University, 3181 S. W. Sam Jackson Park Rd., Portland, OR, 97201: shyngs@ohsu.edu USA

SO Journal of Biological Chemistry, (May 10, 2002) Vol. 277, No. 19, pp. 17139-17146. http://www.jbc.org/. print.
ISSN: 0021-9258.

DT Article

LA English

AB Mutations in the pancreatic ATP-sensitive potassium (KATP) channel subunits sulfonylurea receptor 1 (SUR1) and the inwardly rectifying potassium channel Kir6.2 cause persistent hyperinsulinemic hypoglycemia of infancy. We have identified a SUR1 mutation, L1544P, in a patient with the disease. Channels formed by co-transfection of Kir6.2 and the mutant SUR1 in COS cells have reduced response to MgADP (apprx10% that of the wild-type channels) and reduced surface expression (apprx19% that of the wild-type channels). However, the steady-state level of the SUR1 protein is unaffected. Treating cells with lysosomal or proteasomal **inhibitors** did not improve surface expression of the mutant channels, suggesting that increased degradation of mutant channels by either pathway is unlikely to account for the reduced surface expression. Removal of the RKR endoplasmic reticulum retention/retrieval trafficking motif in either SUR1 or Kir6.2 increased the surface expression of the mutant channel by apprx35 and apprx20%, respectively. The simultaneous removal of the RKR motif in both channel subunits restored surface expression of the mutant channel to the wild-type channel levels. Thus, the L1544P mutation may interfere with normal trafficking of KATP channels by causing improper shielding of the RKR **endoplasmic reticulum retention**/retrieval trafficking **signals** in the two channel subunits.

L6 ANSWER 3 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

AN 2002:298511 BIOSIS

DN PREV200200298511

TI Importance of the gamma-aminobutyric acidB receptor C-termini for G-protein coupling.

AU Gruenewald, Sylvia (1); Schupp, Bettina J.; Ikeda, Stephen R.; Kuner, Rohini; Steigerwald, Frank; Kornau, Hans-Christian; Koehr, Georg

CS (1) Axaron Bioscience AG, Im Neuenheimer Feld 515, D-69120, Heidelberg: gruenewald@axaron.com Germany

SO Molecular Pharmacology, (May, 2002) Vol. 61, No. 5, pp. 1070-1080. http://molpharm.aspetjournals.org/. print.
ISSN: 0026-895X.

DT Article

LA English

AB Functional gamma-aminobutyric acidB (GABAB) receptors assemble from two subunits, GABAB(1) and GABAB(2). This heteromerization, which involves a C-terminal coiled-coil interaction, ensures efficient surface trafficking and agonist-dependent G-protein activation. In the present study, we took a closer look at the implications of the intracellular C termini of GABAB(1) and GABAB(2) for G-protein coupling. We generated a series of C-terminal mutants of GABAB(1) and GABAB(2) and tested them for physical interaction, surface trafficking, coupling to adenylyl cyclase, and G-protein-gated inwardly rectifying potassium channels in human embryonic kidney (HEK) 293 cells as well as on endogenous calcium channels in sympathetic neurons of the superior cervical ganglion (SCG). We found that the C-terminal interaction contributes only partly to the heterodimeric assembly of the subunits, indicating the presence of an additional interaction site. The described **endoplasmic reticulum retention signal** within the C terminus of GABAB(1) functioned only in the context of specific amino acids, which constitute part of the GABAB(1) coiled-coil sequence. This finding may provide a link between the retention signal and its shielding by the coiled coil of GABAB(2). In HEK293 cells, we observed that the two well-known GABAB receptor **antagonists** (S-(R*,R*))-(3-((1-(3,4-dichlorophenyl)ethyl)amino)-2-hydroxypropyl)(cyclohexylmethyl) phosphinic acid (CGP54626) and (+)-(2S)-5,5-dimethyl-2-morpholineacetic acid (SCH50911) CGP54626 and SCH50911 function as inverse agonists. The C termini of GABAB(1) and GABAB(2) strongly influenced agonist-independent G-protein coupling, although they were not necessary for agonist-dependent G-protein coupling. The C-terminal GABAB receptor mutants described here demonstrate that the active receptor conformation is stabilized by the coiled-coil interaction. Thus, the C-terminal conformation of the GABAB receptor may determine its constitutive activity, which could be a therapeutic target for inverse agonists.

L6 ANSWER 4 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3

AN 2002:404932 BIOSIS

DN PREV200200404932

TI Obtaining stem borer-resistant homozygous transgenic lines of Minghui 81 harboring novel cry1Ac gene via particle bombardment.

AU Zeng Qian-Chun; Wu Qian (1); Zhou Kai-Da; Feng De-Jiang (1); Wang Feng; Su Jun; Altosaar, Illimar; Zhu Zhen (1)

CS (1) Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, 100101: zzhu@genetics.ac.cn China

SO Acta Genetica Sinica, (Jun., 2002) Vol. 29, No. 6, pp. 519-524. print. ISSN: 0379-4172.

DT Article

LA Chinese

AB A modified cry1Ac gene was generated by fusing with Lys-Asp-Glu-Lue (KDEL), an **endoplasmic reticulum retention signal** at the 3'-ends, with signal peptide coding sequence of Soybean kunitz trypsin **inhibitor** (SKTI) at the 5'-ends. Vector containing the modified cry1Ac gene coding region flanked by the corn ubiquitin 1 promoter and the nopaline synthase gene (nos) terminator with Hygromycin Phosphotransferase (hpt) gene as a plant selection marker was constructed. The modified cry1Ac gene in which toxic protein targeted to endoplasmic retention was successfully transferred into Minghui 81 (Oryza sativa L. subsp. indica), an elite restoring line of commercial CMS indica hybrid rice, through particle bombardment and obtained fertile transformants. Homozygous transgenic rice lines were obtained in the third generation exploiting self-seed set reproduction and HygromycinB selection. These transgenic lines were confirmed with polymerase chain reaction (PCR) amplification, Southern blotting and ELISA detection. Pest insect-resistant bioassay indicated that some of the homozygous cry1Ac -transgenic rice plants of T2 progeny showed high-level resistance against

striped stem borer (Chilo suppressalis) at field trials.

L6 ANSWER 5 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:2451 BIOSIS
DN PREV200200002451
TI Tissue and cell type specific cleavage of the beta-site APP cleaving enzyme (BACE.
AU Bryant, D. N. (1); McGraw, W. T.; Yang, Y. (1); Shoemaker, J. T.; D'Souza, I. (1); Krohn, A. J. (1); Collin, K. W. (1); Lah, J. J.; Cook, D. G. (1)
CS (1) GRECC, Department of Medicine, V.A. Medical Center, University of Washington, Seattle, WA USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2085. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
AB Recent advances indicate that BACE is responsible for APP beta-secretase cleavage. BACE undergoes a number of post-translational modifications as it transits the secretory pathway. To better understand these processes we examined BACE expression in frontal cortex, cerebellum, pancreas, liver, and skeletal muscle from rat, mouse, and human. Unlike brain, where BACE is expressed primarily as a 70kD holoprotein, peripheral tissue expressed BACE predominantly as a truncated 35kD C-terminal fragment (CTF). Pulse/Chase studies were done to determine if there was a precursor/product relationship between BACE holoprotein and CTF. In BHK and C2 contractile myotube cultures BACE was proteolytically cleaved approximately 3 hours into the chase, producing both N- and C-terminal fragments. CTF formation was blocked in cells expressing BACE with a di-lysine **endoplasmic reticulum retention signal** and by treatment with the vacuolar H+-ATPase **inhibitor**, bafilomycin. This suggests BACE cleavage occurs late in the secretory pathway, likely in endosomal/lysosomal compartments. In contrast, BACE does not form the 35kD CTF in neurons. These findings indicate that tissue-specific BACE proteolysis is a regulated feature of its processing and maturation. Abundant BACE CTF expression in specific tissues suggests that it is biologically relevant and may serve other functions in addition to cleavage of APP.

L6 ANSWER 6 OF 57 WPINDEX (C) 2002 THOMSON DERWENT
AN 2000-618773 [59] WPINDEX
DNN N2000-458590 DNC C2000-185284
TI Novel drug delivery molecule used to deliver drugs to endothelial cells expressing the somatostatin type II receptor, to improve circulation, vision and a neoplasm related health condition.
DC B04 D16 P34
IN GRAUPNER, G
PA (GRAU-I) GRAUPNER G
CYC 91
PI WO 2000053236 A2 20000914 (200059)* EN 37p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000037303 A 20000928 (200067)
EP 1173192 A2 20020123 (200214) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000053236 A2 WO 2000-US6001 20000308; AU 2000037303 A AU 2000-37303

20000308; EP 1173192 A2 EP 2000-916155 20000308, WO 2000-US6001 20000308
FDT AU 2000037303 A Based on WO 200053236; EP 1173192 A2 Based on WO 200053236
PRAI US 1999-123352P 19990308
AB WO 200053236 A UPAB: 20001117
NOVELTY - A drug delivery molecule, comprising a targeting moiety that binds a cell surface receptor, without eliciting an agonistic effect, a routing moiety, and a bioactive molecule coupled to the routing moiety, either of which is coupled to the targeting moiety, is new. Binding of the targeting moiety to the receptor results in cellular uptake of the drug delivery molecule.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a drug delivery molecule having the structure (I)-(IV); and

(2) selectively targeting an endothelial cell located proximal to an anomalous cell, comprising recognizing that the proximal endothelial cell has a detectable amount of a somatostatin type II receptor, and that a non-proximal endothelial cell does not have the receptor, and presenting the proximal endothelial cell with a compound that specifically binds to the somatostatin type II receptor.

BAM = bioactive molecule.

ACTIVITY - Ophthalmological; Cytostatic. No biological data is given.

MECHANISM OF ACTION - None given.

USE - The somatostatin type II receptor specific compound can be administered to an endothelial cell with a detectable amount of the receptor on its surface, and located proximal to tissue having reduced circulation, preferably caused by stenosis of a blood vessel in the brain or heart, to tissue having a focus of macular degeneration, or to tissue having a neoplasm selected from a lymphoma, a sarcoma, an adenocarcinoma, and a teratocarcinoma, improving circulation, vision and a health condition, respectively (claimed).

ADVANTAGE - The drugs are specifically targeted to the diseased cells.

Dwg.0/4

L6 ANSWER 7 OF 57 BIOTECHABS COPYRIGHT 2002 THOMSON DERWENT AND ISI
AN 2001-00154 BIOTECHABS
TI Production of hepatitis B surface antigen in transgenic plants for oral immunization;
hepatitis B virus surface antigen expression in potato tuber for use as edible vaccine
AU Richter L J; Thanavala Y; Arntzen C J; *Mason H S
CS Univ.Cornell-Inst.Plant-Res.; Roswell-Park-Cancer-Inst.
LO Boyce Thompson Institute for Plant Research, Inc., Tower Rod., Ithaca, NY 14853-1801, USA.
Email: hsm7@cornell.edu
SO Nat.Biotechnol.; (2000) 18, 11, 1167-71
CODEN: NABIF ISSN: 1087-0156
DT Journal
LA English
AB Mice fed transgenic potato (Solanum tuberosum) tubers expressing hepatitis B virus surface antigen (HBsAg) showed a primary immune response (increases in HBsAg-specific serum antibody) that was greatly boosted by i.p. delivery of a single subimmunogenic dose of commercial HBsAg vaccine, indicating that plants expressing HBsAg in edible tissues may be a means for oral hepatitis B immunization. To improve expression levels, expression cassettes were constructed in which HbsAg gene expression was driven by the cauliflower-mosaic virus 35S promoter and dual enhancer, and also included: the tobacco-etch virus or tobacco-mosaic virus 5' untranslated region; the 3' region of the Agrobacterium nopaline-synthase gene, soybean (Glycine max) vegetative storage protein gene vspB, or potato protease **inhibitor** II gene; the signal peptide from soybean vspA, optionally with a vacuolar

targeting **signal**; a hexapeptide **endoplasmic reticulum** (ER) **retention signal**; and a Rubisco transit peptide. The most striking improvements resulted from the use of alternative polyA signals and targeting signals designed to enhance integration or retention of HbsAg in the ER of plant cells. (30 ref)

L6 ANSWER 8 OF 57 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
AN 2000:559644 CAPLUS
DN 133:131182
TI Insecticidal fusion protein, its coded gene and method for producing transgenosis strain using said gene
IN Zhu, Zhen; Deng, Chaoyang; Qu, Qiang
PA Genetics Inst., Chinese Academy of Sciences, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 55 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1229087	A	19990922	CN 1999-103430	19990330

AB The disclosed insecticidal fusion protein contains signal peptide at its N-terminal, insecticidal protein, and **endoplasmic reticulum-retention signal** at its C-terminal. The signal peptide is selected from potato patatin signal peptide, pathogenesis-related protein PR signal peptide, and soybean Kunitz type trypsin **inhibitor** (SKTI) signal peptide; the insecticidal protein is selected from Bacillus thuringiensis (Bt) toxoprotein, cowpea trypsin **inhibitor** (CpTI) insect-resistant protein, paddy mercapto- protease **inhibitor** (OC), or bivalent insecticidal protein comprising their fusion proteins; and the signal peptide of the insecticidal protein and **endoplasmic reticulum-retention signal** such as KDEL and HDEL. The expression vector is a plant-transfecting vector, contains one or more insecticidal gene expression box and/or other gene expression box, and the exogenous gene of the expression box is controlled under plant promoter. The plant promoter is selected from CaMV 35S promoter, CLCuV replicase gene promoter, paddy actin promoter, T-DNA mas promoter, maize ubiquitin promoter, and their promoter complexes. The expression vector is used for prepn. of insect-resistant plants such as paddy, maize, wheat, tobacco, cotton, soybean, potato, cabbage, brassica oleracea, and pepper, etc. The transgenosis plant is prepd. by construction of expression vector encoding insecticidal fusion protein, transfecting plant cells with the vector, and culturing the plant cells.

L6 ANSWER 9 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1999:444783 BIOSIS
DN PREV199900444783
TI The nuclear envelope serves as an intermediary between the ER and Golgi complex in the intracellular parasite Toxoplasma gondii.
AU Hager, Kristin M.; Striepen, Boris; Tilney, Lewis G.; Roos, David S. (1)
CS (1) Department of Biology, University of Pennsylvania, Philadelphia, PA, 19104-6018 USA
SO Journal of Cell Science, (Aug., 1999) Vol. 112, No. 16, pp. 2631-2638.
ISSN: 0021-9533.
DT Article
LA English
SL English
AB Morphological examination of the highly polarized protozoan parasite Toxoplasma gondii suggests that secretory traffic in this organism

progresses from the endoplasmic reticulum to the Golgi apparatus using the nuclear envelope as an intermediate compartment. While the endoplasmic reticulum is predominantly located near the basal end of the parasite, the Golgi is invariably adjacent to the apical end of the nucleus, and the space between the Golgi and nuclear envelope is filled with numerous coatomer-coated vesicles. Staining with antiserum raised against recombinant T. gondii beta-COP confirms its association with the apical juxtanuclear region. Perturbation of protein secretion using brefeldin A, microtubule **inhibitors** or dithiothreitol disrupts the Golgi, causing swelling of the nuclear envelope, particularly at its basal end. Prolonged drug treatment leads to gross distention of the endoplasmic reticulum, filling the basal end of the parasite. Cloning and sequencing of the T. gondii homolog of the chaperonin protein BiP identifies the carboxy-terminal amino acid sequence HDEL as this organism's **endoplasmic reticulum-retention signal** . Appending the HDEL motif to a recombinant secretory protein (a chimera between the parasite's major surface protein fusion, P30, and the Green Fluorescent Protein) causes this secretory reporter to be retained intracellularly. P30-GFP-HDEL fluorescence was most intense within the nuclear envelope, particularly at the apical end. These data support a model of secretion in which protein traffic from the endoplasmic reticulum to Golgi occurs via the apical end of the nuclear envelope.

L6 ANSWER 10 OF 57 WPINDEX (C) 2002 THOMSON DERWENT
AN 1998-312418 [27] WPINDEX
DNC C1998-096427
TI New isolated human endoplasmic reticulum retention signal KDEL receptor NHKR - used to develop products for treating e.g. conditions involving defective functioning of the Golgi apparatus, hypercholesterolemia or infections.
DC B04 D16
IN BANDMAN, O; GOLI, S K; HILLMAN, J L
PA (INCY-N) INCYTE PHARM INC
CYC 40
PI WO 9822506 A1 19980528 (199827)* EN 67p
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AT AU BR CA CH CN DE DK ES FI GB IL JP KR MX NO NZ RU SE SG US
AU 9852554 A 19980610 (199843)
US 5824500 A 19981020 (199849)
EP 942933 A1 19990922 (199943) EN
R: BE DE ES FR GB IT NL
US 6103874 A 20000815 (200041)
JP 2002511733 W 20020416 (200242) 73p
ADT WO 9822506 A1 WO 1997-US20666 19971117; AU 9852554 A AU 1998-52554 19971117; US 5824500 A US 1996-753159 19961121; EP 942933 A1 EP 1997-947487 19971117, WO 1997-US20666 19971117; US 6103874 A Div ex US 1996-753159 19961121, US 1998-133735 19980813; JP 2002511733 W WO 1997-US20666 19971117, JP 1998-523730 19971117
FDT AU 9852554 A Based on WO 9822506; EP 942933 A1 Based on WO 9822506; US 6103874 A Div ex US 5824500; JP 2002511733 W Based on WO 9822506
PRAI US 1996-753159 19961121; US 1998-133735 19980813
AB WO 9822506 A UPAB: 19980709
A purified novel human KDEL receptor (NHKR) is claimed comprising an 214 amino acid sequence given in the specification, or fragments. Also claimed are: (1) an isolated and purified polynucleotide sequence (PNS) encoding the NHKR; (2) a PNS which hybridises under stringent conditions to a PNS as in (1); (3) a hybridisation probe comprising a PNS as in (2); (4) an isolated and purified PNS comprising a 1073 bp sequence given in the specification or variants; (5) a PNS which is complementary to a sequence as in (4); (6) a hybridisation probe comprising a PNS as in (5); (7) an expression vector containing a PNS as in (1); (8) a host cell containing a

vector as in (7); (9) a purified antibody which binds specifically to a the NHKR; (10) a purified agonist which specifically binds to and modulates the activity the NHKR; (11) a purified **antagonist** which specifically binds to and inhibits the NHKR.

USE - The NHKR functions as an **endoplasmic reticulum** (ER) **retention receptor**. Vectors expressing NHKR may be administered to increase the level of NHKR in conditions characterised by defective functioning of the Golgi apparatus, low levels of NHKR expression, and diminished antigen processing capacity. **Antagonists** or **inhibitors** of NHKR may be administered to suppress the expression of NHKR for treatment of ER storage diseases including hypercholesterolemia and hypothyroidism. **Antagonists** of NHKR can also be used for the treatment of infections such as those caused by fungal and protozoan organisms such as Saccharomyces cerevisiae and Giardia lamblia. The probes can also be used for detection of PNS encoding NHKR in biological samples by hybridisation assay (the sample may be subjected to PCR prior to analysis) (claimed). The products may be used in diagnosis and drug screening. The cells and vectors may be used to produce NHKR (claimed).

Dwg.0/5

L6 ANSWER 11 OF 57 COPYRIGHT 2002 Gale Group DUPLICATE 6

AN 97:47285 NLDB
TI HIV Gene Therapy "Replication of Primary HIV-1 Isolates Is Inhibited in PM1 Cells Expressing sCD4-KDEL."
SO Gene Therapy Weekly, (10 Feb 1997) .
ISSN: 1078-2842.
PB Charles W Henderson
DT Newsletter
LA English
WC 236

L6 ANSWER 12 OF 57 PROMT COPYRIGHT 2002 Gale Group

AN 97:78712 PROMT
TI HIV Gene Therapy "Replication of Primary HIV-1 Isolates Is Inhibited in PM1 Cells Expressing sCD4-KDEL."
SO AIDS Weekly Plus, (10 Feb 1997) pp. N/A.
ISSN: 1069-1456.
LA English
WC 236

FULL TEXT IS AVAILABLE IN THE ALL FORMAT

AB Degar, S.; Johnson, J.E.; Boritz, E.; Rose, J.K. Virology, December 15, 1996;226(2:424-429.

not multimeric

According to the authors' abstract of an article published in Virology, "Expression or a soluble CD4 molecule (sCD4-KDEL containing a specific **retention signal** for the **endoplasmic reticulum** was shown previously to block propagation of the HIV-1(MN prototype strain in a transformed T-cell line. However, the virus present in HIV-1-infected individuals is more closely represented by primary HIV-1 isolates which, unlike the HIV-1(MN strain, have not been adapted to growth in cell lines. To determine if sCD4-KDEL could block replication of primary isolates we used the PM1 cell line that has been shown to propagate primary isolates without adaptation. Here we show that the replication of four primary HIV-1 isolates was strongly inhibited in PM1 cells that expressed sCD4-KDEL under control of the HIV-1 LTR. infection with primary HIV-1 isolates induced sCD4-KDEL expression driven by the LTR. HIV-1 spread was dramatically reduced, and reverse transcriptase activity in the cell culture supernatants was greatly diminished. sCD4-KDEL, therefore, represents a potent **inhibitor** of HIV-1 replication for gene therapy-based approaches for the treatment

of AIDS." The corresponding author for this study is: JK Rose, Yale Univ, Sch Med, Dept Pathol, 310 Cedar St, New Haven, CT 06510 USA. For subscription information for this journal contact the publisher: Academic Press Inc Jnl-Comp Subscriptions, 525 B St, Ste 1900, San Diego, CA 92101-4495.

L6 ANSWER 13 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
AN 1997:36998 BIOSIS
DN PREV199799343401
TI Replication of primary HIV-1 isolates is inhibited in PM1 cells expressing sCD4-KDEL.
AU Degar, Steven; Johnson, J. Erik; Boritz, Eli; Rose, John K. (1)
CS (1) Dep. Cell Biol., Yale Univ. Sch. Med., 310 Cedar St., New Haven, CT 06510 USA
SO Virology, (1996) Vol. 226, No. 2, pp. 424-429.
ISSN: 0042-6822.
DT Article
LA English
AB Expression of a soluble CD4 molecule (sCD4-KDEL) containing a specific **retention signal** for the **endoplasmic reticulum** was shown previously to block propagation of the HIV-1-MN prototype strain in a transformed T cell line. However, the virus present in HIV-1-infected individuals is more closely represented by primary HIV-1 isolates which, unlike the HIV-1-MN strain, have not been adapted to growth in cell lines. To determine if sCD4-KDEL could block replication of primary isolates we used the PM1 cell line that has been shown to propagate primary isolates without adaptation. Here we show that the replication of four primary HIV-1 isolates was strongly inhibited in PM1 cells that expressed sCD4-KDEL under control of the HIV-1 LTR. Infection with primary HIV-1 isolates induced sCD4-KDEL expression driven by the LTR, HIV-1 spread was dramatically reduced, and reverse transcriptase activity in the cell culture supernatants was greatly diminished. sCD4-KDEL, therefore, represents a potent **inhibitor** of HIV-1 replication for gene therapy-based approaches for the treatment of AIDS.

L6 ANSWER 14 OF 57 DUPLICATE 8
AN 96:28867 AQUASCI
DN ASFA1 1996 26-16506
TI Cloning and characterization of a cDNA encoding the collagen-binding stress protein hsp47 in zebrafish
AU Pearson, D.S.; Kulyk, W.M.; Kelly, G.M.; Krone, P.H.
CS Dep. Anatomy and Cell Biol., Univ. Saskatchewan, Saskatoon, SK S7N 5E5, Canada
SO DNA CELL BIOL., (1996) vol. 15, no. 3, pp. 263-272.
ISSN: 1044-5498.
DT Journal
FS ASFA1
LA English
SL English
AB Hsp47 is a major stress-inducible protein that is localized to the endoplasmic reticulum of avian and mammalian cells and is thought to act as a molecular chaperone specific for the processing of procollagen. Although hsp47 is coordinately expressed together with several collagen types, and vertebrate embryos are known to express collagen genes in complex spatial and temporal patterns, limited information is available regarding the function or regulation of hsp47 during early embryonic development. We have initiated an examination of hsp47 in the zebrafish, Danio rerio, which offers a number of features that make it attractive as

a model developmental system with which to examine the expression and function of hsp47. A polymerase chain reaction (PCR)-based cloning strategy was used to isolate a hsp47 cDNA from an embryonic zebrafish cDNA library. The deduced translation product of the cDNA is a 404-amino-acid polypeptide that is 72% identical to chicken, 64% identical to mouse and rat, and 69% identical to human hsp47. The protein contains a typical hydrophobic **signal** sequence, an RDEL **endoplasmic reticulum retention signal**, and a serine protease **inhibitor** signature sequence, all of which are characteristic of hsp47 in higher vertebrates. Thus, it is likely that hsp47 in zebrafish is also localized to the endoplasmic reticulum and may play a similar role to its counterpart in higher vertebrates. Northern blot analysis revealed that the hsp47 gene is expressed at relatively low levels in embryos during normal development but is strongly induced following exposure to heat shock at the gastrula, midsomitogenesis, 2-day, and 3-day larval stages. The level of induction was much higher than has previously been reported in chicken and mouse cells.

L6 ANSWER 15 OF 57 AGRICOLA
AN 96:31263 AGRICOLA
DN CAT10714688
TI Peptides 1994 : proceedings of the Twenty-Third European Peptide Symposium, September 4-10, 1994, Braga, Portugal.
AV DNAL (QD431.E8 1994)
SO 1995 lxvi, 934 p. : ill., ports. (some col.) ; 25 cm
Publisher: Leiden : ESCOM, 1995.
Meeting Info.: European Peptide Symposium; Braga, Portugal; 1994.
ISBN: 9072199219.
NTE Includes bibliographical references and indexes.
Cycle of solid phase synthesis / R.C. Sheppard -- Synthesis of amino acids selectively labelled with stable isotopes / U. Ragnarsson ... [et al.] -- Azabenzotriazole (HOAt) derivatives as superior coupling reagents for peptide synthesis / F. Albericio ... [et al.] -- Impprovements in the chemical synthesis of proteins / K. Barlos ... [et al.] -- Chemical synthesis of proteins: design of appropriate methodology / R. Ramage ... [et al.] -- Chemoselective ligation methods in TASP design / G. Tuchscherer ... [et al]. Engineering of peptide dendrimers using unprotected peptide segments as building blocks / J.C. Spetzler, C. Rao and J.P. Tam -- Industrial production of an oxytocin **antagonist**: synthetic approaches to the development of a multi-kilogram scale solution synthesis / C. Johansson ... [et al.] -- Solution synthesis of human midkine, a 121-residue peptide with five disulfide bonds / T. Inui ... [et al.] -- Design of potent hexapeptide endothelin **antagonists** stable to proteolysis / W.L Cody ... [et al.].
Phosphorylated glycopeptide templates as high affinity ligands for the Man-6-P receptor / M. Meldal ... [et al] -- Direct characterization of supramolecular complexes of polypeptides and proteins by electrospray mass spectrometry / M. Przybylski ... [et al] -- Structure-function relationships of antimicrobial dermaseptins / K. Hani, P. Nicolas and A. Mor -- Isolation and structural analysis of a novel beta-defensin hBD-1 from human hemofiltrate / K.W. Bensch ... [et al] -- Disruption of helix-helix interactions in biologically relevant proteins: HIV-1 inhibition by gp41 fragments / W.M. Kazmierski and J. McDermed -- Design and synthesis of chimerical proteins containing a natural alpha/beta scorpion fold / C. Vita ... [et al.] -- Solution structure of the N-terminal SH3 domain of Grb2 by 1H NMR and identification of its ligand binding region / N. Goudreau ... [et al.] -- Preferred conformation of Ac8c peptides / E. Benedetti ... [et al.] -- Proline-rich region from maize gamma-zein adopts a left-handed amphipathic structure that may act as a **signal** for its **retention** in the **endoplasmic reticulum** / I Dalcol ... [et al.].
CY Netherlands

DT Bibliography; (MONOGRAPH)
FS Non-U.S. Imprint other than FAO
LA English

L6 ANSWER 16 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9
AN 1992:365231 BIOSIS
DN BA94:47281
TI MOLECULAR CLONING OF A MOUSE 47-KDA HEAT-SHOCK PROTEIN HSP47 A COLLAGEN-BINDING STRESS PROTEIN AND ITS EXPRESSION DURING THE DIFFERENTIATION OF F9 TERATOCARCINOMA CELLS.
AU TAKECHI H; HIRAYOSHI K; NAKAI A; KUDO H; SAGA S; NAGATA K
CS DEP. CELL BIOL., CHEST DISEASE RESEARCH INST., KYOTO UNIV., KYOTO 606, JPN.
SO EUR J BIOCHEM, (1992) 206 (2), 323-329.
CODEN: EJBCAI. ISSN: 0014-2956.
FS BA; OLD
LA English
AB A 47-kDa heat-shock protein (HSP47) is a major collagen-binding stress protein residing in the endoplasmic reticulum, and is assumed to be a molecular chaperone specific to collagen. Two-dimensional gel electrophoresis and immunoprecipitaton studies showed that the expression of HSP47 was significantly induced during the differentiation of mouse teratocarcinoma F9 cells by treatment with retinoic acid alone or with retinoic acid and dibutyryladenosine 3',5'-phosphate. The induction of type-IV collagen was also observed during F9-cell differentiation. For further analysis, we cloned cDNA encoding mouse HSP47 from a cDNA library of BALB/c 3T3 cells and performed Northern-blot analysis. The cDNA contained a signal sequence at the N-terminus and an **endoplasmic -reticulum-retention signal**, RDEL, at the C-terminus. An homology search revealed that mouse HSP47, as well as chick HSP47, belonged to the serine protease **inhibitor** superfamily. While chick HSP47 mRNa was 4.5 kb with a long (2-kb) 3' untranslated region, mouse and human HSP47 mRNA were 2.5 kb, with a 0.8-kb 3' untranslated region. Northern-blot analysis revealed that the concurrent induction of HSP47 and type-IV collagen during F9-cell differentiation and the transient induction of HSP47 after heat shock was regulated at the level of mRNA accumulation. These results suggested that HSP47 was closely related to collagens in terms of its expression as well as in its functional relevance.

L6 ANSWER 17 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
AN 1991:501068 BIOSIS
DN BA92:124028
TI A COLLAGEN-BINDING PROTEIN IN THE ENDOPLASMIC RETICULUM OF MYOBLASTS EXHIBITS RELATIONSHIP WITH SERINE PROTEASE INHIBITORS.
AU CLARKE E P; CATES G A; BALL E H; SANWAL B D
CS DEP. BIOCHEMISTRY, UNIVERSITY WESTERN ONTARIO, LONDON, ONTARIO, CAN. N6A 5C1.
SO J BIOL CHEM, (1991) 266 (26), 17230-17235.
CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB Several cDNA clones encoding a 46-kDa collagen-binding glycoprotein (gp46) from rat skeletal myoblasts were isolated and sequenced. The cDNA encoded a 17-amino acid signal peptide and a 400-amino acid mature protein, containing three potential N-linked oligosaccharide attachment sites. The cDNA sequence of gp46 shows 93% identity in the coding region with J6, a retinoic acid-inducible gene coding for a protein of unknown function described from embryonal carcinoma F9 cells. The first 41 NH2-terminal amino acids of the predicted J6 sequence are, however, different from the

gp46 sequence as a result of a 7-base pair insertion in the gp46 cDNA. In addition, the NH2-terminal amino acid sequence of hsp47, a collagen-binding protein found in chick embryos fibroblasts, shows 64% identity to gp46 over 36 residues. Interestingly, this alignment begins 10 residues inward from the first amino acid in the mature form of gp46. A significant sequence similarity was observed between gp46 and members of the serine protease **inhibitor** (serpin) family. Unlike other serpins, however, gp46 is both a heat shock and a collagen-binding protein and is localized to the lumen of the endoplasmic reticulum, as suggested by the presence of the RDEL sequence at the COOH terminus. This sequence is similar to other proposed **endoplasmic reticulum retention signals**.

L6 ANSWER 18 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 11
AN 1991:431117 BIOSIS
DN BA92:87282
TI HSP47 A TISSUE-SPECIFIC TRANSFORMATION-SENSITIVE COLLAGEN-BINDING HEAT SHOCK PROTEIN OF CHICKEN EMBRYO FIBROBLASTS.
AU HIRAYOSHI K; KUDO H; TAKECHI H; NAKAI A; IWAMATSU A; YAMADA K M; NAGATA K
CS DEP. CELL BIOL., CHEST DISEASE RESEARCH INST., KYOTO UNIV., KYOTO 606-01, JPN.
SO MOL CELL BIOL, (1991) 11 (8), 4036-4044.
CODEN: MCEBD4. ISSN: 0270-7306.
FS BA; OLD
LA English
AB We report the isolation and characterization of a cDNA clone encoding HSP47, a transformation -sensitive heat shock protein that binds to collagen. A cDNA library was prepared from total RNA isolated from heat-shocked chicken embryo fibroblasts and screened by using oligonucleotide mixtures prepared on the basis of the N-terminal amino acid sequence of biochemically purified HSP47. The cDNA insert contained 3,278 bp, which encoded a 15-amino-acid signal peptide and mature protein coding region consisting of 390 amino acid residues; it also included part of the 5' noncoding region and a long 3' noncoding region. The deduced amino acid sequence revealed an RDEL sequence at the C terminus, which is a variant of the KDEL retention **signal** for **retention** of proteins in the **endoplasmic reticulum**. Northern (RNA) blot analyses and nuclear run-on assays established that the induction of HSP47 by heat shock and its suppression after transformation of chicken embryo fibroblasts by Rous sarcoma virus are regulated at the transcriptional level. A homology search revealed that this protein belongs to the serpin family, the superfamily of plasma serine protease **inhibitors**. Although structurally homologous to the serpins, HSP47 lacks the active site thought to be essential for the inhibition of proteases and does not appear to bind to intracellular proteases. HSP47 is the first heat shock protein found to be a member of the serpin superfamily. Conversely, it is the first serpin family member that is not secreted from cells, which could be explained by acquisition of the RDEL retention signal during evolution.

L6 ANSWER 19 OF 57 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 12
AN 1991:46761 BIOSIS
DN BA91:25042
TI CARBOXYL TERMINAL KDEL-MODIFIED CYSTATIN C IS RETAINED IN TRANSFECTED CHO CELLS.
AU JOHANSEN T E; VOGEL C K; SCHWARTZ T W
CS LAB. MOL. ENDOCRINOL., UNIV. DEP. CLINICAL CHEM., RIGSHOSPITALET 6321, BLEGDAMSVEJ 9, DK-2100 COPENHAGEN, DENMARK.
SO BIOCHEM BIOPHYS RES COMMUN, (1990) 172 (3), 1384-1391.
CODEN: BBRCA9. ISSN: 0006-291X.

FS BA; OLD
LA English
AB The significance of a C-terminal tetrapeptide, Lys-Asp-Glu-Leu (KDEL), as a **retention signal** for the **endoplasmic reticulum** was studied using cystatin C, a general thiol protease **inhibitor**, as the receptor protein. Clones of CHO clels were analyzed after stable transfection with eukaryotic expression vectors encoding either cystatin C, KDEL extended cystatin C, or cystatin C extended with a control sequence. It is concluded that cystatin C with the KDEL tetrapeptide as a C-terminal extension is retained intracellularly without apparent accumulation of the molecule.

L6 ANSWER 20 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAY70697 peptide DGENE
TI Isolated nucleic acids encoding human attractin polypeptides useful for enhancing immune responses -
IN Duke-Cohan J S; Schlossman S F
PA (DAND) DANA FARBER CANCER INST INC.
PI WO 2000015651 A1 20000323 120p
AI WO 1999-US20948 19990914
PRAI US 1998-100137 19980914
DT Patent
LA English
OS 2000-271373 [23]
AB The patent discloses four forms of human attractin polypeptides which enhance immune response by promoting macrophage and monocyte spreading in the presence of T cells. These include soluble attractin-1 and -2 and membrane attractin-1 and -2. These various forms of attractin are encoded by alternatively spliced mRNA molecule transcribed from a single gene. The present sequence is a **retention signal** for **endoplasmic reticulum** (ER) which can be used to direct attractin to a specified intracellular location. Attractin can be used to enhance immune response in immunosuppressed patients such as those undergoing chemo- and radio-therapy treatment for cancer or those suffering from common variable immunodeficiency syndrome. The protein may also be used to screen modulators (agonists and **antagonists**) of immune responses which may also be used to regulate immune reactions. Attractin antibodies can be used to inhibit immune response in transplant recipients or patients afflicted with autoimmune disease.

L6 ANSWER 21 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAW40035 Peptide DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB The present sequence represents a human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The DNA sequence was isolated from a lung cDNA library, and was first identified in the partial cDNA, Incyte Clone 809200p, through a computer-generated search for amino acid sequence alignments. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 22 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAW48812 Protein DGENE
TI New isolated human endoplasmic reticulum retention signal KDEL receptor NHKR - used to develop products for treating e.g. conditions involving defective functioning of the Golgi apparatus, hypercholesterolemia or infections
IN Bandman O; Goli S K; Hillman J L
PA (INCY-N) INCYTE PHARM INC.
PI WO 9822506 A1 19980528 68p
AI WO 1997-US20666 19971117
PRAI US 1996-753159 19961121
DT Patent
LA English
OS 1998-312418 [27]
AB This polypeptide comprises NHKR, a novel human KDEL **receptor** that functions as an **endoplasmic reticulum** (ER) **retention receptor**. Its amino acid sequence was deduced from a consensus DNA sequence (see AAV32447) derived from overlapping and extended Incyte clones. It shows chemical and structural homology to human KDEL receptors GI 31218 (74% identity) and GI 119543 (71% identity). The invention also provides genetically engineered expression vectors and host cells comprising nucleic acid sequences encoding NHKR that are used in a claimed method for producing NHKR, as well as probes and primers, antibodies, agonists and **antagonists** of NHKR. Vectors expressing NHKR may be administered to increase the level of NHKR in conditions characterised by defective functioning of the Golgi apparatus, low levels of NHKR expression, and diminished antigen processing capacity. **Antagonists** or **inhibitors** of NHKR may be administered to suppress the expression of NHKR for treatment of ER storage diseases, e.g. hypercholesterolemia and hypothyroidism. **Antagonists** of NHKR can also be used for the treatment of infections such as those caused by Saccharomyces cerevisiae and Giardia lamblia. Antibodies that specifically bind NHKR can be used in diagnostic assays.

L6 ANSWER 23 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAZ58442 DNA DGENE
TI Novel screen comprising a pool of vectors with randomly modified nucleotide sequences, useful for identifying modulators of enzyme activity useful for selecting antibiotic agents -
IN Halkier T; Jespersen L; Jensen A
PA (MEBI-N) M & E BIOTECH AS.
PI WO 2000005406 A1 20000203 136p
AI WO 1999-DK408 19990716
PRAI DK 1998-956 19980720
US 1998-94868 19980729
DT Patent
LA English
OS 2000-182719 [16]
AB The present sequence is that of a primer used in a PCR amplification designed to add an **endoplasmic reticulum** **retention signal** in frame to the C-terminus of the

chymotrypsin **inhibitor** 2A (CI-2A) in plasmid pCMVbipepER/CI-2A (see AAZ58432). The invention relates to improvements in CellScreen technology that encompass screening in prokaryotic as well as eukaryotic cells, and which can be used to identify and/or prepare peptides or RNAs capable of modulating the activity in vivo of target enzymes in eukaryotic cells. Previously unknown interactions between targets and ligands can be identified. Enzyme **inhibitor** structures such as CI-2A are used as scaffolds to display intracellularly potentially biologically active peptides or RNAs in a stable form. Preparation of a medicinal product is based on initial identification of targets or ligands using the methods of the invention.

L6 ANSWER 24 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAZ58441 DNA DGENE
TI Novel screen comprising a pool of vectors with randomly modified nucleotide sequences, useful for identifying modulators of enzyme activity useful for selecting antibiotic agents -
IN Halkier T; Jespersen L; Jensen A
PA (MEBI-N) M & E BIOTECH AS.
PI WO 2000005406 A1 20000203 136p
AI WO 1999-DK408 19990716
PRAI DK 1998-956 19980720
US 1998-94868 19980729
DT Patent
LA English
OS 2000-182719 [16]
AB The present sequence is that of a primer used in a PCR amplification designed to add an **endoplasmic reticulum retention signal** in frame to the C-terminus of the chymotrypsin **inhibitor** 2A (CI-2A) in plasmid pCMVbipepER/CI-2A (see AAZ58432). The invention relates to improvements in CellScreen technology that encompass screening in prokaryotic as well as eukaryotic cells, and which can be used to identify and/or prepare peptides or RNAs capable of modulating the activity in vivo of target enzymes in eukaryotic cells. Previously unknown interactions between targets and ligands can be identified. Enzyme **inhibitor** structures such as CI-2A are used as scaffolds to display intracellularly potentially biologically active peptides or RNAs in a stable form. Preparation of a medicinal product is based on initial identification of targets or ligands using the methods of the invention.

L6 ANSWER 25 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09953 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 26 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09952 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of
the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 27 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09969 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 28 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09968 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of
the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 29 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09967 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 30 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09966 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 31 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09965 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 32 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09964 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 33 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09963 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 34 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09962 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 35 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09961 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 36 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09960 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 37 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09959 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 38 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09958 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 39 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09957 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 40 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09956 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 41 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09955 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 42 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09954 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 43 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09981 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 44 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09980 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 45 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09979 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 46 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09978 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 47 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09977 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 48 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09976 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 49 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09975 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 50 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09974 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 51 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09973 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 52 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09972 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 53 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09971 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of

the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 54 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09970 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB Sequences AAV09952-81 represent overlapping partial cDNA clones that make up a cDNA encoding a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The cDNA sequences were isolated from a human lung cDNA library. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 55 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09982 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB The present sequence appears in the specification. The specification describes a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein

disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 56 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV09951 cDNA DGENE
TI Human protein di:sulphide isomerase - used for the production of correctly folded recombinant proteins and in diagnosis
IN Braxton S M; Murry L E
PA (INCY-N) INCYTE PHARM INC.
PI WO 9743426 A1 19971120 78p
AI WO 1997-US8115 19970514
PRAI US 1996-650275 19960516
DT Patent
LA English
OS 1998-086528 [08]
AB The present sequence encodes a novel human protein disulphide isomerase (PIDH). This type of isomerase is found in membrane-bound eukaryotic compartments such as the endoplasmic reticulum, and facilitates disulphide bond exchange as well as correct glycosylation. The present sequence was isolated from a lung cDNA library, and was first identified in the partial cDNA, Incyte Clone 809200p, through a computer-generated search for amino acid sequence alignments. PIDH has 39% identity to the Caenorhabditis elegans thioredoxin, and 16% identity to the alfalfa protein disulphide isomerase. PDIH has a conserved **endoplasmic reticulum retention signal** at the 3' end of the peptide, and lacks potential glycosylation sites. The cDNA encoding PIDH, or fragments of it, as well as antibodies against PIDH can be used in the diagnosis of conditions or disease associated with protein disulphide isomerase (PDI) expression. The protein and its agonists may be used for the in vitro production and folding of recombinant, therapeutic human proteins. Antisense DNA and other **inhibitors** of the protein can be delivered to blood or liver cells to reduce PDI expression and reduce the secretion of PDI and the tissue destruction attributed to PDI secreted platelets and hepatocytes.

L6 ANSWER 57 OF 57 DGENE (C) 2002 THOMSON DERWENT
AN AAV32447 DNA DGENE
TI New isolated human endoplasmic reticulum retention signal KDEL receptor NHKR - used to develop products for treating e.g. conditions involving defective functioning of the Golgi apparatus, hypercholesterolemia or infections
IN Bandman O; Goli S K; Hillman J L
PA (INCY-N) INCYTE PHARM INC.
PI WO 9822506 A1 19980528 68p
AI WO 1997-US20666 19971117
PRAI US 1996-753159 19961121
DT Patent
LA English
OS 1998-312418 [27]
AB This polynucleotide codes for NHKR (see AAW48812) a novel human KDEL **receptor** that functions as an **endoplasmic reticulum** (ER) **retention receptor**. It is a consensus sequence derived from overlapping and/or extended Incyte clones 364214 (from cDNA library PROSNOT01), 350031 (LVENNOT01), 38492 (HUVENOB01) and 1856520 (PROSNOT18); Incyte clone 364214 was initially identified from the PROSNOT01 library through a computer-generated search for amino acid sequence alignments. The invention also provides genetically engineered expression vectors and host cells comprising

nucleic acid sequences encoding NHKR used in a claimed method for producing NHKR, as well as probes and primers, antibodies, agonists and **antagonists** of NHKR. Vectors expressing NHKR may be administered to increase the level of NHKR in conditions characterised by defective functioning of the Golgi apparatus, low levels of NHKR expression, and diminished antigen processing capacity. **Antagonists** or **inhibitors** of NHKR may be administered to suppress the expression of NHKR for treatment of ER storage diseases, e.g. hypercholesterolemia and hypothyroidism. **Antagonists** of NHKR can also be used for the treatment of infections such as those caused by Saccharomyces cerevisiae and Giardia lamblia. The probes can also be used for detection of polynucleotide sequences encoding NHKR in biological samples by hybridisation assay (the sample may be subjected to PCR prior to analysis) (claimed). The products may also be used in diagnosis and drug screening.

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